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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/695,769	10/25/2000	Darwin J Prockop	9598-101U2(99-0356)	4022
7590 11/19/2003			EXAMINER	
Morgan, Lewis & Bockius, L.L.P			SHUKLA, RAM R	
1701 Market Street			ART UNIT	
Philadelphia, PA 19103			PAPER NUMBER	

1632

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/695,769

Applicant(s)

PROCKOP ET AL.

Examiner

Ram R. Shukla

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-41 is/are pending in the application.
- 4a) Of the above claim(s) 30 and 37-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-29 and 31-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 October 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8-28-2003 has been entered.
2. Claims 30 and 37-41 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.
3. This application contains claims 30 and 37-41 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
4. Claims 1-29 and 31-36 are under consideration.
5. Applicants in their response indicated a request for an interview with the examiner, however Examiner Shukla was not contacted regarding the interview.

### ***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 1-21 are rejected under 35 U.S.C. 102(b) as anticipated by Bruder et al (Journal of Cellular Biochemistry 64:278-294, 1997) for reasons of record set forth in the previous office action of 6-5-02 and 2-26-2003.

### ***Response to Arguments***

Applicant's arguments filed 8-28-2003 have been fully considered but they are not persuasive. Applicants' arguments that Bruder does not teach each and every element of claims 1-21 are not persuasive. Applicants have argued that the method of Bruder et al is not a method of inducing or enhancing proliferation rather it is an art accepted method of isolating adherent cells. Applicants' arguments are not persuasive because the steps of Bruder et al's method are same as that recited instantly therefore the methods would result in induction of proliferation. Applicants have argued that the cells of Bruder et al are not isolated cells. Again these arguments are not persuasive because the claims as instantly presented do not recite as to isolated from other cells types or from where and since any cells that are in cell culture are isolated, Bruder et al's cells are isolated cells. Next applicants have argued that Bruder et al does not teach less than 50 cells per square centimeter as recited in claim 12. Again applicants' arguments are not persuasive because the claimed method (claim 12) recites "less than about 50 cells.." which would encompass the claimed limitation. As noted in the previous office action, the only two embodiments of the claimed invention are- isolated human marrow stromal cells that have density of less than 50 cells per square

centimeter of growth surface and incubating the growth surface in the presence of growth promoting conditions and this limitation is taught by the reference cited. Applicants' arguments regarding the definition of the human marrow stromal cells in the specification, it is noted that claims are given broadest possible interpretation and the description is not read into claim language when considering the claimed invention, Bruder et al teaches isolated bone marrow cells that have approximately 1 marrow stromal cell in  $10^5$  cells, which represents 100 cells in a 60 cm<sup>2</sup> dish. Accordingly, the art of Bruder et al would meet the limitations of the claimed invention.

8. Claims 1-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuznetsov et al (Journal of Bone and Mineral Research 12:1335-1347, 1997) for reasons of record set forth in the previous office action of 6-5-02 and 2-26-2003.

### ***Response to Arguments***

Applicant's arguments filed 8-28-2003 have been fully considered but they are not persuasive. Applicants have argued that the reference does nowhere describes any process to isolated marrow stromal cells from the rest of the bone marrow milieu, however, these arguments are not persuasive, as discussed above in paragraph #6, since the claimed invention does not recite any such limitation. Applicants have further argued that the range for Kuznetsov et al is 7-3500 and lower density is less than and the upper density is greater than the claimed invention. However, these arguments are not persuasive because the claimed density is encompassed in the 7-3500 range. Applicants' arguments that Kuznetsov et al does not teach isolated population of MSCs is not persuasive because the claimed as recited does not exclude the presence of other cells in the culture.

### ***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuznetsov et al (Journal of Bone and Mineral Research 12:1335-1347, 1997) in view of Azizi et al (Proc. Natl. Acad. Sci. USA 95:3908-3913, 1998) for reasons of record set forth in the previous office action of 6-5-02 and 2-26-2003.

### ***Response to Arguments***

Applicant's arguments filed 8-28-2003 have been fully considered but they are not persuasive. Applicants' arguments regarding Kuznetsov et al's teaching have been discussed above in paragraph #7. Applicants have discussed the teachings of Kuznetsov as how it differs from the teachings of the instant application, however, these arguments are irrelevant because the issue is obviousness and claims under consideration are 22-23 that recite addition of growth factors to the culture of cells. It is noted that why Kuznetsov et al practiced their method is irrelevant because the issue is the method steps and not why the method was practiced. As discussed in the previous office actions, adding PDGF-AA to the culture medium would have been obvious due to the effect of PDGF-AA on the growth rate of marrow stromal cells as taught by Azizi et al.

11. Claims 1, 24-29 and 31-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuznetsov et al and Azizi et al as applied to claims 22-23 above, and further in view of Greenberger et al (US Patent No 5,766,950, 6-16-1998) and Prockop (Science 276:71-74, 1997) for reasons of record set forth in the previous office action of 6-5-02 and 2-26-2003.

***Response to Arguments***

Applicant's arguments filed 8-28-2003 have been fully considered but they are not persuasive. Applicants have reiterated their arguments above Kuznetsov et al and Azizi et al. These were responded to in the previous paragraph. Regarding the issue of combining of the teaching of the cited arts, applicants argue that Greenberger et al teaches a substantially different conditioned media and method for expanding stromal cells. It is noted that the teaching of Greenberger et al that is relevant in the instant case is the addition of conditioned medium and not the purpose why Greenberger practiced his method. At the time of the invention, Greenberger taught the method of adding conditioned medium for growing stromal cells with a reasonable expectation of success. Therefore, adding growth factors or any other culture condition has nothing to do with the source of the marrow cells and conditions could be applied to cells of different sources. Applicants' do not provide any evidence as to why an artisan would not have had reasonable expectation of success in combining the conditions because an artisan of ordinary skill in the art will have the conditions for the marrow stromal cells from different sources and in fact Prockop article reviews overall state of the art of stem cells and therefore, all the different types of tissues that can be derived from marrow stromal cells are discussed in this article (see the entire article). Applicants have argued that even if one or all of the molecules listed by Prockop are secreted by MSCs and influence the proliferation of MSCs, the list is not exhaustive and does not offer the skilled artisan a reasonable expectation of success in developing the conditioned medium claimed. Applicants' arguments are not persuasive because recited claims do not provide any more exhaustive list by listing range of molecular weight of nutrients. Additionally, applicants did not provide any evidence that the conditioned medium of the cited references will lack such nutrients.

12. No claim is allowed.

**Action Is Final, First Action Following Request for Continued Examination under 37 CFR 1.114**

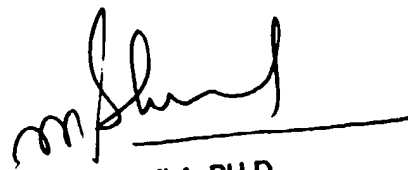
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All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a) A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

Ram R. Shukla, Ph.D.  
Primary Examiner  
Art Unit 1632



**RAM R. SHUKLA, PH.D.**  
**PRIMARY EXAMINER**